034

Syncope after myocardial infarction. Changes of the results of programmed ventricular stimulation during the last 26 years

Béatrice Brembilla-Perrot, Bérivan Azman, Nicolas Sadoul, Hugues Blangy, Olivier Claudon, Karim Djaballah, Pierre Louis, Olivier Selton, Lucian Muresan, Sonia Magalhes, Pierre Yves Zinzius, Arnaud Terrier De La Chaise
CHU of Brabois, Cardiologie, Vandoeuvre Les Nancy, France

Ventricular tachycardia (VT) may explain syncope after myocardial infarction (MI) and is in this case is associated with a high risk of sudden death, mainly in association with low left ventricular ejection fraction (LVEF). Programmed ventricular stimulation (PVS) remains the main method to look for VT. The purpose of the study was to look for the changes of the population referred for PVS for unexplained syncope after MI during the last 26 years.

Methods: 346 patients were recruited for unexplained syncope after MI between 1982 and 2008: 76 patients (group I) were studied between 1982 and 1989; 151 patients (group II) were studied between 1990 and 1999 and 119 patients (group III) were studied between 2000 and 2008. ECG and 24 hour Holter monitoring did not indicate a possible cause of syncope. LVEF was evaluated in all patients by echocardiography. PVS was systematic with the same protocol (up to 3 extrastimuli in 2 sites of right ventricle).

Results: Clinical and electrophysiological data were similar between groups I and II but differed significantly in group III: age was higher in group III (68±12 years) than in group I (64±11) and II (65±12) ($p < 0.009$); LVEF was higher in group III (45±13%) than in group I (41±16) and II (42±13) ($p<0.008$). PVS was more frequently negative in group III (74%) than in group I (43%) and II (54 %) ($p<0.001$). Monomorphic VT < 270 b/min was less frequently induced in group III (16 %) than in group I (30 %) and II (26 %) ($p<0.01$). Ventricular flutter (VT > 270/min) and ventricular fibrillation were less frequently induced in group III (9 %) than in group I (26 %) and II (19 %) ($p<0.05$).The changes could be related to the ICD implantation recommendations and to recanalization of occluded coronary artery, which is systematic in recent MI since 2000 (38 % in group III, 27 % in groups I and II) ($p < 0.05$).

Conclusions: Clinical data and results of PVS in patients admitted for unexplained syncope after MI infarction were identical between 1982 and 199 and have changed since 2000; patients are older and had relatively preserved LVEF. Therefore, the induction of a ventricular tachyarrhythmia is rarer than before the year 2000.

January 15th, Friday 2010

035

Comparison of Omeprazole and Pantoprazole Influence on Clopidogrel Effect of a High 150 mg Maintenance Dose: the Proton pomp inhibitors and Clopidogrel Association (PACA) prospective, randomized study

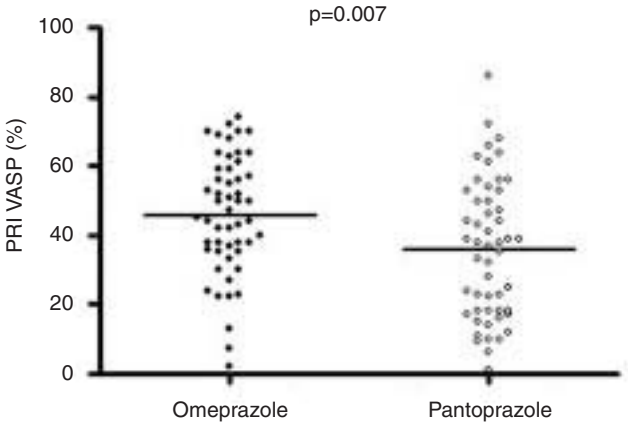
Thomas Cuisset (1), Corinne Frere (2), Jacques Quilici (3), Raphael Poyet (4), Laurent Bali (3), Pierre Morange (4), Marie Christine Alessi (2), Jean Louis Bonnet (3)
(1) CHU Timone, Service de Cardiologie Interventionnelle, Marseille, France – (2) Inserm, U626, Faculté de Médecine Timone, Laboratory of Haematology, Marseille, France – (3) CHU Timone, Department of Cardiology, Marseille, France – (4) Inserm, U626, Faculté de Médecine, Laboratoire d'Hématologie, Marseille, France

Objective: To compare the effect of two Proton Pomp Inhibitors (PPI) on platelet response to clopidogrel after coronary stenting for Non ST Elevation Acute Coronary Syndrome (NSTE ACS).

Background: Use of omeprazole has been reported to decrease significantly the clopidogrel antiplatelet effect because of cytochrome P450 interaction. As all PPIs are metabolized by CYP2C19, but to a varying degree, we hypothesized that the reported negative omeprazole-clopidogrel drug interaction may not be due to a class effect.

Methods and Results: 104 patients undergoing coronary stenting for NSTE ACS were prospectively included and randomized to omeprazole or pantoprazole 20 mg. They received at discharge 75 mg aspirin and 150 mg clopidogrel. Platelet reactivity index VASP was used to assess clopidogrel response and ADP-induced aggregation for platelet reactivity (ADP-Ag). After one month, patients receiving pantoprazole had a significantly better platelet response to clopidogrel as assessed with the PRI VASP: 36±20 % vs 48±17 %, p=0.007. We identified more clopidogrel non responders in the omeprazole group than in the pantoprazole group: 44% vs 23%, p=0.04, OR 2.6 [1.2-6.2]. Conversely, we did not observe any significant difference in platelet reactivity with ADP-Ag between omeprazole and pantoprazole groups: 52±15 % and 50±18 % respectively, p=0.29.

Conclusion: The present findings suggest the preferential use of pantoprazole compared to omeprazole in patients receiving clopidogrel to avoid any potential negative interaction with CYP2C19.



Clopidogrel response according to PPI

036

Comparison of the Angiographic Myocardial Blush Grade with Delayed Enhanced Cardiac Magnetic Resonance for the assessment of Microvascular Obstruction in Acute Myocardial Infarctions

Jacques Vicente, Nathan Mewton, Pierre Croisille, Patrick Staat, Eric Bonnefoy, Michel Ovize, Didier Revel
Hopital Cardiovasculaire Louis Pradel, Cardiologie, Bron, France

Background: Myocardial Blush Grade (MBG) and cardiac magnetic resonance (CMR) are both imaging tools that can assess myocardial reperfusion after primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI).

Objectives: We studied the relation between MBG and gadolinium-enhanced CMR for the assessment of microvascular obstruction (MVO) in patients with acute ST-elevated myocardial infarction (STEMI) treated by primary PCI.

Material and Methods: MBG was assessed in 39 patients with initial TIMI 0 STEMI successfully treated by PCI, resulting in TIMI 3 flow grade and complete ST-segment resolution. These MBG values were related to MVO determined by CMR, performed between 2 and 7 days after PCI. Left ventricular (LV) volumes were determined at baseline, and at 6-month follow up.

Results: No statistical relation was found between MBG and MVO extent at CMR (p=0.63). Regarding MBG 0 and 1 as a sign of MVO, the sensitivity and specificity of these scores were respectively 53.8% and 75%. In this study, CMR determined MVO was the only significant LV remodeling predicting factor (_=31.8; p=0.002), whatever the MBG status was.

Conclusion: MBG underestimates MVO after an optimal revascularization in AMI compared to CMR. This study suggests the superior accuracy of delayed enhanced magnetic resonance (DEMR) over MBG for the assessment of myocardial reperfusion injury which is needed in clinical trials where the principal endpoint is the reduction of infarct size (IS) and MVO.

037

The relative contribution of the CYP2C19*2 polymorphism in the low responsiveness to clopidogrel in the VASP-02 study

Boris Aleil (1), Laurent Jacquemin (2), Fabien De Poli (3), Michel Zaehringer (1), Jean-Philippe Collet (4), Gilles Montalescot (4), Catherine Léon (5), Jean-Pierre Cazenave (5), Marie-Claude Dickele (3), Jean-Pierre Monassier (2), Christian Gachet (5)
(1) Clinique de l'Orangerie, Cardiologie, Strasbourg, France – (2) Hôpital Emile Muller, Service de Cardiologie, Mulhouse, France – (3) Centre Hospitalier Général, Service de Cardiologie, Haguenau, France – (4) Hôpital Pitié-Salpêtrière (AP-HP), Institut de Cardiologie and INSERM U856, Paris, France – (5) Institut National de la Santé et de la Recherche Médicale U.311, Etablissement Français du Sang – Alsace, Strasbourg, France

The CYP2C19*2 genetic variant is known to contribute to low responsiveness to clopidogrel treatment, leading to a higher rate of cardiovascular events. Systematic identification of the 2C19*2 carriers to predict the individual patient's response to clopidogrel is a matter of debate.

Data of the VASP-02 study comparing patients' responsiveness to 75 and 150 mg/day maintenance dose of clopidogrel (Aleil et al., J Am Coll Cardiol Intv 2008) were reanalyzed by determining the 2C19*2 carrier status of the patients. Platelet reactivity index (PRI) was determined using the VASP method. A PRI>69 % defines low responsiveness to clopidogrel.

In the 37 non responder patients, 42.4 % were 2C19*2 carriers versus 22.0 % in the responder patients (p=0.022). After multivariate analysis, 2C19*2 polymorphism and high body weight were two independent predictors of high PRI (odds ratio [95% confidence interval] 3.39 [1.06-10.84] p=0.039 and 3.14 [1.19-8.30] p=0.021) respectively. Increasing the maintenance dose of clopidogrel from 75 to 150 mg/day in non responder patients resulted in a significant decrease of PRI from 76.4±4.6 to 62.8±10.4 % (p<0.01) in 2C19*2 carriers and from 76.1±5.3 to 60.8±13.4 % (p<0.01) in non carriers. The mean decrease of PRI after doubling the dose was not significantly different between carriers and non carriers of the genetic variant (-13.6±9.3 and -15.3±11.8 % p=0.39, respectively).

CYP2C19*2 is an important determinant of the responsiveness to clopidogrel while other independent factors such as body weight also are involved. Hyporesponsiveness in 2C19*2 carriers can be easily overcome by doubling the maintenance dose of clopidogrel. Thus, combined functional pharmacodynamic monitoring and genetic determination of CYP profile should help improve patient's responsiveness to clopidogrel.

038

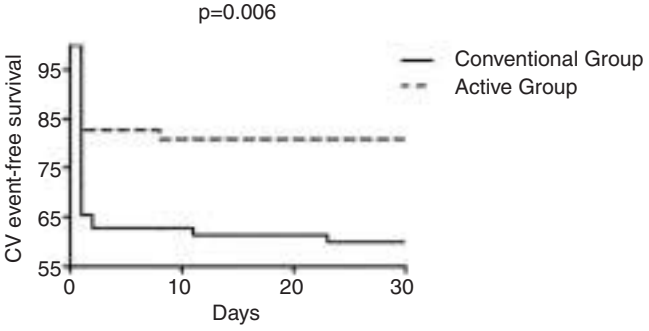
Glycoprotein IIbIIIa Inhibitors Improve Clinical Outcome after Coronary Stenting in Clopidogrel non Responders: a Prospective, Randomized Study

Thomas Cuisset (1), Corinne Frere (2), Jacques Quilici (3), Raphael Poyet (4), Laurent Bali (3), Pierre E Morange (2), Marie Christine Alessi (2), Jean Louis Bonnet (3)
(1) CHU Timone, Service de Cardiologie Interventionnelle, Marseille, France – (2) Inserm, U626, Faculté de Médecine Timone, Laboratory of Haematology, Marseille, France – (3) CHU Timone, Department of Cardiology, Marseille, France – (4) Inserm, U626, Faculté de Médecine, Laboratoire d'Hématologie, Marseille, France

Introduction: Numerous biological studies have reported inter-individual variability in platelet response to clopidogrel with clinical relevance. High Post treatment platelet reactivity (ADP-induced aggregation >70%) has been proposed to define Non response to clopidogrel. We assessed in clopidogrel non responders undergoing elective percutaneous coronary intervention (PCI) the benefit of adjusted antiplatelet therapy with glycoprotein IIbIIIa (GPIIbIIIa) antagonist administration during PCI for one month clinical outcome.

Methods and Results: 149 clopidogrel non-responders referred for elective PCI were prospectively included and randomized to "conventional group" (n=75) or "active group" with GPIIbIIIa antagonist (n=74). All patients received 250 mg aspirin and 600 mg clopidogrel before PCI and platelet testing. The rate of CV events at one month was significantly lower in the "active group" than in the "conventional group": 19% (n=14) vs. 40% (n=30), p=0.006, [OR (95%CI): 2.8(1.4-6.0)]. No patient in either group had post procedural TIMI major bleeding or required transfusions.

Conclusion: The present study suggested benefit of tailored antiplatelet therapy during elective PCI with GPIIbIIIa antagonist for clopidogrel non responders without increased bleeding risk.



039

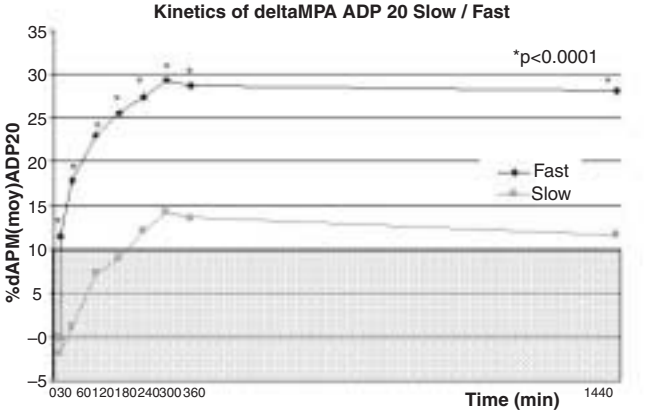
Slow Response to Clopidogrel Predicts Low Response

Anne Bellemain-Appaix, Gilles Montalescot, Johanne Silvain, Olivier Bathelemy, Farzin Beygui, Jean-Philippe Collet – Hopital Pitié Salpetrière, Cardiologie, Paris, France

Objectives: To determine if the speed of response to clopidogrel loading predicts the final degree of response to clopidogrel.

Background: Fast inhibition of platelet aggregation is important in the setting of ACS and PCI, but its relation to the final degree of inhibition is not well established.

Methods: We performed a post-hoc analysis of ALBION, which included 103 NSTE-ACS patients randomised to 300, 600 or 900mg LD of clopidogrel. Early kinetic profiles of ADP 20µmol/l Maximal Platelet Aggregation (MPA) and deltaMPA (with baseline sample as reference) were studied, with 8 time points within the 24 hours following loading. Low response was defined as deltaMPA<10%



Relationship between onset of action and magnitude